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Clinical Study

Preoperative steroid use and the incidence of perioperative complications in patients undergoing craniotomy for definitive resection of a malignant brain tumor

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ABSTRACT

We studied the impact of preoperative steroids on 30 day morbidity and mortality of craniotomy for definitive resection of malignant brain tumors. Glucocorticoids are used to treat peritumoral edema in patients with malignant brain tumors, however, prolonged ($\geqslant$10 days) use of preoperative steroids as a risk factor for perioperative complications following resection of brain tumors has not been studied comprehensively. Therefore, we identified 4407 patients who underwent craniotomy to resect a malignant brain tumor between 2007 and 2012, who were reported in the National Surgical Quality Improvement Program, a prospectively collected clinical database. Metastatic brain tumors constituted 37.5% (n = 1611) and primary malignant gliomas 62.5% (n = 2796) of the study population. We used logistic regression to assess the association between preoperative steroid use and perioperative complications before and after 1:1 propensity score matching. Patients who received steroids constituted 22.8% of the population (n = 1009). In the unmatched cohort, steroid use was associated with decreased length of hospitalization (odds ratio [OR] 0.7; 95% confidence interval [CI] 0.6–0.8), however, the risk for readmission (OR 1.5; 95% CI 1.2–1.8) was increased. In the propensity score matched cohort (n = 465), steroid use was not statistically associated with any adverse outcomes. Patients who received steroids were less likely to stay hospitalized for a protracted period of time, but were more likely to be readmitted after discharge following craniotomy. As an independent risk factor, preoperative steroid use was not associated with any observed perioperative complications. The findings of this study suggest that preoperative steroids do not independently compromise the short term outcome of craniotomy for resection of malignant brain tumors.

1. Introduction

Glucocorticoids are used in patients with metastatic brain tumors and malignant gliomas to manage neurological symptoms secondary to vasogenic peritumoral edema [11,20,36]. Systemic steroid use is associated with several side effects including hyperglycemia and insulin resistance, immunosuppression and poor wound healing and venous thromboembolism, among others [20,35]. In spite of the frequency of their use and the potential to increase the incidence of conditions that may influence operative outcomes [23], the role of steroids as a preoperative risk factor for morbidity and mortality in patients undergoing craniotomy for definitive resection of malignant brain tumors has not been studied comprehensivel [4,13–18,21,22,30,37,45,46,49].

Using the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) database, a validated, prospectively collected clinical database, we examined the impact of preoperative steroid use on the 30 day morbidity and mortality of patients who underwent craniotomy for resection of malignant brain tumors.

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2. Methods

2.1. Database

The ACS-NSQIP database was queried for patients who underwent cranial surgery for definitive resection of a malignant brain tumor between January 2007 and December 2012. This study was approved by The Cleveland Clinic Institutional Review Board.

ACS-NSQIP is a prospective clinical database of perioperative variables collected from nearly 400 community and academic hospitals. The data is collected without the knowledge of the surgeon, by a trained surgical clinical reviewer from de-identified consenting patients according to annually reviewed standardized definitions [2,27,39]. Accurate and reproducible, the ACS-NSQIP achieves >95% 30 day outcomes and follow-up across consecutive cycles [27,28].

2.2. Study population

We identified 4426 patients who underwent surgery to resect a malignant brain tumor (Fig. 1). Patients who only underwent a biopsy were excluded from this analysis. We excluded patients who received preoperative transfusion (n = 16) or had septic shock prior to surgery (n = 3) because inclusion of these patients skewed the unmatched analyses and hindered our ability to match patients based on propensity score. Our final study population consisted of 4407 patients with malignant brain tumors who underwent craniotomy for definitive resection. Of these, 1009 patients received steroids preoperatively. In the ACS-NSQIP, preoperative steroid use is recorded as systemic use of corticosteroid medications for a chronic medical condition for at least 10 days within the 30 days preceding the index surgery [3]. The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes for malignant glioma were 191.0 to 191.9, and for brain metastasis 198.3. Patients with any and all other primary and secondary tumor diagnoses were excluded. The primary and secondary current procedural terminology (CPT) codes used in the ACS-NSQIP to identify a craniotomy with definitive resection of malignant neoplasm (by ICD-9-CM code) are detailed in Figure 1. It is to be noted, for example, that a malignant glioma resected in concert with removal of epidural or subdural electrode array was noted as a separate procedure (CPT 61535) or from the cerebellopontine angle (CPT 61520), or as part of a skull base approach (CPT 61580), combined with definitive resection of an intradural tumor (CPT 61601). In all patients, the primary ICD-9-CM code based on the final pathological diagnosis was used as the discriminating factor, rather than the code used to define the procedure as described by the surgeon in the operative report [3].

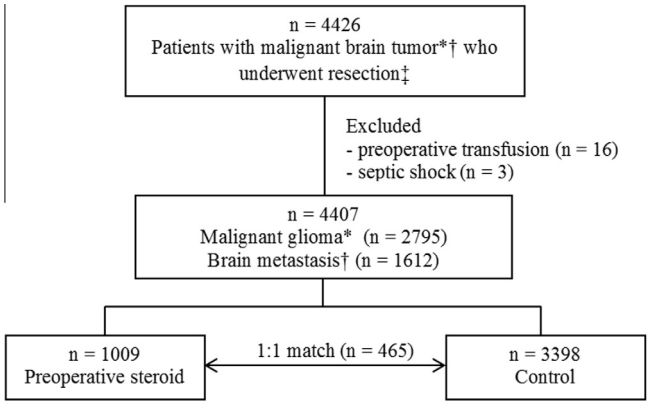

Fig. 1. Craniotomy for definitive resection of a malignant brain tumor, patient selection criteria. *International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes indicative of malignant gliomas were 191.0–191.9. † ICD-9-CM code indicative of brain metastasis was 198.3. ‡Current procedural terminology codes indicative of craniotomy for resection of brain tumor were: 61510, 61518, 61520, 61521, 61526, 61530, 61537, 61538, 61539, 61540, 61580, 61581, 61582, 61583, 61584, 61585, 61586, 61590, 61591, 61592, 61595, 61596, 61597, 61598, 61600, 61601, 61605, 61606, 61607, 61608, 61609, 61610, 61611, 61612, 61613, 61615, 61616, 61618, 61619.

2.3. Covariates

We compared baseline characteristics, including demographic variables, preoperative laboratory values, medical and surgical comorbidities in patients who did or did not receive preoperative steroids (Table 1).

2.4. Primary outcomes

We examined the following outcome measures after surgery: (1) prolonged length of hospital stay (LOS) defined as LOS longer than the third quartile (>75% of the sample, which was 8 days); (2) minor complications including superficial surgical site infection, urinary tract infection, deep venous thrombosis or thrombophlebitis; (3) major complications including deep incision surgical site infection, organ or space surgical site infection, wound disruption, pneumonia, unplanned intubation, pulmonary embolism, >48 hour postoperative ventilator-assisted respiration, progressive renal insufficiency, acute renal failure, cerebrovascular accident with neurological deficit, coma of >24 hours, cardiac arrest requiring cardiopulmonary resuscitation, myocardial infarction, sepsis, septic shock, and/or 30 day return to the operating room; (4) any complication, defined as having at least one minor or major complications; (5) unanticipated return to the operating room, defined as return to the operating room for any major surgical procedure; (6) discharged with continued care, defined as discharge to a non-home care facility (exempting those who were initially admitted from such facilities); (7) readmission, defined as any unplanned readmission to the same or another hospital within 30 days of the index surgery; (8) death within 30 days of the index surgery.

2.5. Statistical analyses

We used propensity score analysis, defined in general as the probability of exposure given a set of observed covariates, to control for selection bias [38]. We determined a propensity score for each patient using multivariate logistic regression with preoperative steroid use as a dependent variable and a selected group of covariates as independent variables, namely, admission from home, functional status, American Society of Anesthesiologists (ASA) classification, and preoperative chemo- and/or radiation therapy. Subsequently, we matched patients who received preoperative steroids to those who did not according to each patient's propensity score using the 1:1 greedy matching technique [10]. Propensity score matching allows for a balanced distribution of observed covariates which achieves the same effect as randomization in a prospective study [5–7]. To ensure covariate balance was achieved after matching, we used an absolute standardized difference [5–7]. An absolute standardized difference >0.20 was considered significant [5–7]. The use of significance tests such Pearson's chi-squared or Fisher's exact test is ill-advised because in such statistical measures the p value depends on the sample size which is inadvertently smaller in the matched cohort, thereby, translating to a larger p value. This may result in the false notion that covariate balance was achieved upon matching [5–7]. Nevertheless, since readers are often accustomed to these values, we present p values generated from Pearson's chi-squared test for categorical variables